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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,646	02/22/2002	Robert Norman Rice	37921-2	1954

7590 10/21/2002

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EXAMINER

GUNTER, DAVID R

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 10/21/2002

4

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/081,646

Applicant(s)

RICE ET AL.

Examiner

David R. Gunter

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

Status of the Application

1. The applicant's petition to make special, filed February 22, 2002 in paper number 3, was granted on September 20, 2002.

Specifcation

2. The use of numerous trademarks, including Dynabead® (page 20, line 25) has been noted in this application. The trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 3 and 5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claims 3 and 5 recite the additional limitation to claims 1 and 4 that

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the biotin-labeled RNA transcripts are eluted from the streptavidin-coated iron beads prior to determining the quantity of RNA present. At the top of page 21 the specification states that “the present invention further proposes to modify Dynabead[®] immobilization to enable labeled transcripts to be cleaved or eluted off the bead by the incorporation of a cleavable or otherwise labile linker between, for example, a UTP and a biotin label or between a Dynabead[®] and streptavidin.” Example 18 (page 65, first paragraph) states that the “process is modified to enable the streptavidin Dynabead[®] captured biotin UTP labeled transcripts to be cleaved or eluted.” Despite these assertions that the method could be modified to incorporate a labile linker to allow elution of the captured RNA, the specification does not demonstrate that such a modification was made by the applicants or that the modification allowed elution of the captured RNA.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1 and 2 are rejected under 35 U.S.C. 102(a) as being anticipated by Patrone, et al., Biotechniques 29(5):1012-1017, November 2000 (hereinafter referred to as “Patrone”). The instant application recites a method for determining the rate of transcription in a composition of cells comprising lysing cells and purifying the nuclei that comprise transcriptional units and their attached nascent RNA strands. The nuclei are placed on ice and then incubated in conditions

that permit transcription and in the presence of biotin-16-UTP to provide a population of biotin-labeled nascent transcripts. The biotin-labeled nascent transcripts are immobilized onto streptavidin-labeled iron beads, and are then purified by magnetic separation of the beads from solution. The level of specific biotin-labeled RNA transcripts is determined by subjecting the transcripts to PCR.

Patrone discloses a method identical to that of the instant application. The method of Patrone includes all of the steps of the instant application: lysing cells, purifying nuclei, and putting the nuclei on ice (page 1014, left column, second paragraph), incubating the nuclei under conditions that allow transcription of RNA in the presence of biotin-16-UTP (page 1014, left column, third paragraph), immobilizing the biotin-labeled RNA transcripts onto streptavidin-coated beads (page 1012, right column, third paragraph), purifying the transcripts by magnetic separation of the beads from solution (page 1014, left column, last paragraph), and quantitative PCR of specific RNA transcripts (page 1014, center column, second paragraph).

Patrone does not specifically disclose that the streptavidin coated beads contain iron. However, Patrone does identify the beads as Dynabeads M-280 manufactured by Dynal Biotech (page 1014, left column, last paragraph). The on-line catalog for Dynal Biotech (www.dynalbiotech.com/dynal/index.html) states that Dynabeads M-280 are “superparamagnetic,” and both the web site and the Patrone reference disclose the use of a magnet to purify the beads from solution. The examiner notes that the use of iron beads was well known to those of ordinary skill in the art at the time the application was filed, and that the Patrone reference and the Dynal Biotech catalog clearly indicate that the beads must contain iron or a functionally equivalent material.

Regarding Claim 2, Patrone also discloses the embodiment in which the cells are mammalian cells. Patrone uses two human neuroblastoma cell line (page 1012, right column, last paragraph).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patrone. As described above, Patrone discloses a method that includes all of the steps of the instant application: lysing cells, purifying nuclei, and putting the nuclei on ice (page 1014, left column, second paragraph), incubating the nuclei under conditions that allow transcription of RNA in the presence of biotin-16-UTP (page 1014, left column, third paragraph), immobilizing the biotin-

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labeled RNA transcripts onto streptavidin-labeled iron beads (page 1012, right column, third paragraph), purifying the transcripts by magnetic separation of the beads from solution (page 1014, left column, last paragraph), and quantitative PCR of specific RNA transcripts (page 1014, center column, second paragraph).

Patrone does not specifically teach a kit comprising the buffers, diluents, and enzymes required to perform the method. However, it would have been obvious to one of ordinary skill in the art at the time the application was filed to create a kit for the practice of a known method by preparing and packaging all of the necessary reagents along with appropriate instructions for the completion of the method. Kits were well known in the art at the time the application was filed, and one of ordinary skill would have been motivated to create such a kit because of the time and effort saved by including all of the necessary components in a single unit and because of the commercial potential for the sale of such a kit.

The method of Claim 5 is not limiting on the kit components because the recited buffers, diluents, reagents, and enzymes were known by those of ordinary skill in the art to be useable in other methods such as rtPCR, DNA sequencing, etc.

6. Claims 3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patrone. As described above, Patrone discloses a method that includes all of the steps of the instant application: lysing cells, purifying nuclei, and putting the nuclei on ice (page 1014, left column, second paragraph), incubating the nuclei under conditions that allow transcription of RNA in the presence of biotin-16-UTP (page 1014, left column, third paragraph), immobilizing the biotin-labeled RNA transcripts onto streptavidin-labeled iron beads (page 1012, right column, third

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paragraph), purifying the transcripts by magnetic separation of the beads from solution (page 1014, left column, last paragraph), and quantitative PCR of specific RNA transcripts (page 1014, center column, second paragraph). The method of Claim 1 is rejected as anticipated by Patrone, and the kit of Claim 4 is rejected as being unpatentable over Patrone as described above.

Claims 3 and 5 recite the additional limitation to Claims 1 and 4 that the biotin-labeled RNA transcripts are eluted from the iron beads prior to their quantification. The examiner notes that numerous methods of eluting biotin-labeled molecules away from streptavidin were known in the art at the time the application was filed. These methods include heating the biotin-streptavidin pair to 65°C for five minutes in a solution of 10mM EDTA and 95% formamide at pH 8.2. It would have been obvious to one of ordinary skill in the art at the time the application was filed to adapt the method of Patrone to include the elution of the RNA from the streptavidin-coated beads so that the eluted RNA could be used for a variety of methods such as *in vitro* translation without the interference of the iron bead.

Conclusion

7. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David R. Gunter whose telephone number is (703) 308-1701. The examiner can normally be reached on 9:00 - 5:00 M - F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the

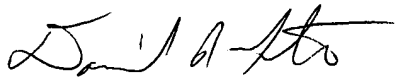
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organization where this application or proceeding is assigned are (703) 746-9212 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0198.



David R. Gunter, DVM, PhD
October 16, 2002



W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600